BLOOD PRESSURE-DEPENDENT CHANGES IN PLASMA VOLUME, GLYCOCALYX AND PLATELET FUNCTION DURING ANAESTHESIA

CLINICAL AND EXPERIMENTAL STUDIES

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Sahlgrens aula, Sahlgrenska Universitetssjukhuset, Göteborg, den 4 juni 2021, klockan 13.00

av Tor Damén

Fakultetsopponent:
Professor Hanne Berg Ravn
Syddansk Universitet, Danmark

Avhandlingen baseras på följande delarbeten

I. Damén T, Reinsfelt B, Redfors B, Nygren A. *Pressure-dependent changes in haematocrit and plasma volume during anaesthesia, a randomised clinical trial.* Acta Anaesthesiol Scand. 2016:60(5):560-568

II. Damén T, Saadati S, Forssell-Aronsson E, Hesse C, Bentzer P, Ricksten SE, Nygren A. *Effects of different mean arterial pressure targets on plasma volume, ANP and glycocalyx-A randomized trial.* Acta Anaesthesiol Scand. 2021:65(2):220-227

III. Damén T, Kolsrud O, Dellgren G, Hesse C, Ricksten SE, Nygren A. *Atrial natriuretic peptide does not degrade the endothelial glycocalyx: a secondary analysis of a randomized porcine model.* Accepted for publication, Acta Anaesthesiol Scand. 2021

IV. Singh S, Damén T, Dellborg M, Jeppsson A, Nygren A. *Intraoperative infusion of noradrenaline improves platelet aggregation in patients undergoing coronary artery bypass grafting: a randomized controlled trial. J. Thromb. Haemost.* 17: 657–665

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

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Blood pressure-dependent changes in plasma volume, glycocalyx and platelet function during anaesthesia – Clinical and experimental studies

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Abstract

Background: Worldwide, more than 300 million surgeries are performed each year. General anaesthesia provides the surgical patient with a state of controlled loss of sensation and awareness. It is common that general anaesthesia causes hypotension. Anaesthesia-induced hypotension is associated with haemodilution and increased plasma volume (PV). The increased PV could potentially release atrial natriuretic peptide (ANP) that is suspected to degrade the endothelial glycocalyx (EG) layer.

Aims: To explore physiological and pathophysiological mechanisms resulting from anaesthesia-related hypotension we: 1) investigated the magnitude and dynamics of PV expansion secondary to anaesthesia induction; 2) assessed whether anaesthesia induction-related increase in PV could be attenuated by maintaining the mean arterial pressure (MAP) at pre-induction levels with norepinephrine (NE) infusion; 3) evaluated the consequences of anaesthesia induction-related PV expansion on the release of ANP and its effects on the EG. We also investigated whether exogenous administration of ANP caused degradation of the EG. Finally, we investigated the effect of NE infusion on platelet function and clot formation.

Methods: We conducted two prospective, randomised, single-centre studies on patients that underwent elective coronary artery bypass grafting (CABG). The patients were randomised to maintain pre-induction MAP (intervention group) or MAP 60 mm Hg (control group) by titration of NE. Baseline PV was measured by ^{125}I-albumin and the change in PV was calculated from the change in haematocrit (Hct). Changes in Mid Regional-pro Atrial Natriuretic Peptide (MR-proANP) and EG-components were measured.

In a prospective, randomised, blinded, experimental study, 20 pigs were randomised to receive an infusion of either ANP or NaCl. Changes in EG components, Hct, calculated PV and colloid osmotic pressure (COP) were measured.

Platelet aggregation was assessed with impedance aggregometry and clot formation with rotational thromboelastometry in study IV.

Results: Lower MAP, (60 mm Hg) secondary to anaesthesia induction increased the PV by 12%, while the PV increased by 2,6% in the intervention group with maintained pre-operative MAP. MR-proANP increased in the group with lower MAP but no degradation of the EG was detected. There was no increase in EG components secondary to an infusion of ANP, but the PV decreased. Intraoperative NE infusion improved platelet aggregation and clot formation.

Conclusions: Haematocrit decreased and plasma volume increased shortly after anaesthesia induction caused hypotension. The increase in plasma volume could be prevented by maintaining pre-induction blood pressure levels with a norepinephrine infusion. No ANP-induced degradation of the EG was detected. Norepinephrine could contribute to a better perioperative haemostasis.

Keywords: Anaesthesia, blood pressure, hypotension, norepinephrine, haematocrit, plasma volume, atrial natriuretic peptide, glycocalyx, platelet aggregation

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